The relationship between poor adherence and HbA1c and weight changes in patients with type 2 Diabetes

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Background

- Despite the arsenal of available treatment options, a large proportion of patients with type 2 diabetes (T2D) have inadequate glycemic control.
- Poor adherence is often seen in chronic diseases
- In diabetes, 50% of patients do not take their medications as prescribed by the physician
- Poor adherence is associated with a lack in achieving glycemic targets, resulting in potentially avoidable morbidity and mortality.
- Poor adherence not only affects HbA1c, but also weight
- Poor adherence to insulin will give less reduction of HbA1c but less weight increase ➔ positive balance?
- Poor adherence to metformin/SGLT/DPP4/GLP-1 will give less weight decrease
- Poor adherence results in less immediate drug costs. Cost of complications are far away in time ➔ positive balance?

Objectives

- The objective of our study was to measure the impact of poor medication adherence on HbA1c and weight levels in T2D patients.

Methods

- A systematic literature review of publications reporting percent change in HbA1c or weight change per quantitative measure of adherence (see next bullet points). The change in HbA1c reported in each study for 100% adherent patients or per every 25% and 10% reduction in adherence level was estimated directly from the available results, or assumed to be linear and figures were extrapolated accordingly. Changes in weight in kg per 10% reduction in adherence were taken from studies reporting both data points.
- Proportion of Days Covered (PDC), which is estimated as the ratio between the number of days in a period "covered" and the total number of patients in that period covered
- Medication Possession Ratio – MPR: Continuous variable: assessing from the first to the last prescription record
- Reporting percentage of change in relationship to percentage of adherence was the key outcome

Results

- The search strategy and hits are shown in table 1.
- 14 publications on HbA1c and 2 on weight were included after titles and abstract evaluation[1,2,4,5,6,7,8,9,10,11,12,13,14,15]
- The 14 studies on HbA1c are shown in table 2.
- The weighted average of all findings was used to account for sample size differences.
- For every 25% and 10% decrement in adherence, the impact on HbA1c was reduced by 0.20% and 0.08%, respectively.
- Finally 1 study on weight loss was withheld. The weight differences between poorly adherent and adherent (>80%), and between very adherent (>90) and very poorly adherent were reported.
- Using the affect on >80 and >90% it was calculated that for every 10% reduction in the adherence the change in weight with GLP-1 RA, DPP-4 and SU is attenuated by at least -0.64, -0.16 and +0.02 Kg respectively (Table 3)[3].

Table 1: Search strategy and hits

Search	Add to builder	Query	Items found
#6	Add	Search (#1 and #3)	182
#5	Add	Search (#1 and #4 and #2)	11
#4	Add	Search ((Glucagon-like peptide-1 [Abstract]) OR (GLP-1 [Abstract])).ab.	116434
#3	Add	Search ((HbA1c [Abstract]) OR (Glycohemoglobin [Abstract]) OR (Glycated hemoglobin [Abstract]) OR (glycaemic [Abstract]))	116434
#2	Add	Search ((body mass index[Abstract]) OR (BMI [Abstract]) OR (Weight[Abstract]))	2028358
#1	Add	Search (diabetes[Title] AND type 2[Title] AND (adherence [Title])	1142

Table 2: Relationship between HbA1c and HbA1c

Study ID	Country/ N	Treatments	Adherence 10%	Adherence 25%	Adherence 100%
Rhee	US /1,263	OAD/INS(40%)	-0.14%	-0.34%	-1.36%
Krapek	US / 301	OAD/INS(34%)	-0.13%	-0.33%	-1.32%
Aikens	US /287	OAD/INS(40%)	-0.06%	-0.16%	-0.64%
Wang	CH /182	ADM	-0.16%	-0.39%	-1.55%
Di Bonaventura	US / 1198	INS Analogs	-0.17%	-0.42%	-1.68%
Schectman	US /810	OADs	-0.19%	-0.48%	-1.90%
		OADs	-0.13%	-0.33%	-1.30%
Pladevall	US / 677	MET	-0.14%	-0.35%	-1.40%
Lawrence	US / 2,070	MET	-0.04%	-0.40%	-1.60%
		SU	-0.24%	-0.60%	-2.40%
Rozenfeld	US / 249	OADs	-0.10%	-0.25%	-1.00%
Horswell	US / 56,181	OADs	-0.09%	-0.22%	-0.88%
Busyman	US / 1321	Liraglutide	-0.08%	-0.20%	-0.81%
McAdam	US / 477	DM	-0.13%	-0.33%	-1.30%
Wright	UK / 34181	1st line monotherapy	-0.06%	-0.15%	-0.60%
Eby	US / 48226	OADs	-0.07%	-0.18%	-0.72%
Weighted average			**-0.08%**	**-0.20%**	**-1.85%**

Table 3: Relationship between drug adherence and weight decrease/increase[3]

Adherence classification	GLP-1 Weight change (kg)	DPP4 Weight change (kg)	SU Weight change (kg)
Adherence PDC >80%	-3.77	-1.18	0.85
Very adherent PDC >90%	-4.41	-1.02	0.87
Impact of adherence on weight			
10% increase on adherence	-0.64	-0.16	0.02
1% change on adherence	-0.064	-0.016	0.002

Limitations

- The major limitations of MPR and PDC are that they measure prescriptions collected and not the use of medicines which may differ (patients may have obtained the drug in the pharmacy but not taken it).
- Very few studies on weight.
- Most of the studies that reported the association between HbA1c and adherence were US based.
- Instead of meta-analytic approach to pool the data, weighted average was used, due to the large heterogeneity of study populations.
- It is important to refer that many of the figures used as representing 100% adherence, were actually taken from the adherent definition used by each of the studies. By this, we mean that, for instance, if adherent patients are defined as having PDC>80% we use this value to represent 100% adherence, since no better evidence is available from the literature. This methodology was also applied in studies reporting other adherence scales.

Conclusions

Poor adherence leads to a lower reduction of HbA1c level, but also to a reduced weight loss or weight gain depending on the anti-diabetes treatment evaluated. These findings should be considered when conducting cost-effectiveness analysis in T2D.

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